UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,256	07/23/2004	Takehiko Kitamori	2004_1163A	3964

513 7590 08/24/2006

WENDEROTH, LIND & PONACK, L.L.P.
2033 K STREET N. W.
SUITE 800
WASHINGTON, DC 20006-1021

EXAMINER	
LUM, LEON YUN BON	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/502,256	KITAMORI ET AL.	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 9, 2006 has been entered.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harrison et al (US 6,432,290 B1) in view of Eteshola et al (Sensors and Actuators B, 2001).

Harrison et al reference teaches a microfluidic substrate (i.e. enzyme immunoassay chip) with buffer inlets 33 and 33a leading into a chamber (i.e. reaction liquid leading-in flow passage part), trapping zone 35 and exit channel 37 (i.e. reaction flow passage part), and collection channel 40 (i.e. detection flow passage part), wherein the chambers and channels are fluidly connected in sequence (i.e. successively connected with each other; reaction flow passage part and the detection flow passage part are arranged so that a majority of enzyme reaction products produced by antigen-antibody reactions with an enzyme in the reaction flow passage part reach the detection flow passage part so as to produce increased signal strength). See column 17, line 39

to column 18, line 7; and Figure 9. In addition, Harrison et al teach that trapping zone 35 includes side channel 34 that pack and unpack the zone with solid phase extraction material (i.e. inlet part for bead-bodies), and that weir 6f in between trapping zone 35 and exit channel 37 (i.e. flow stopping part). See column 17, lines 55-67 and Figure 9. Furthermore, Harrison et al teach that beads are unable to traverse the weirs because the distance from the top of the weirs to the bottom of the plate is less than the diameter of the individual particles (i.e. flow stopping part has a channel depth shallower than that of the reaction flow passage to stop the flow of bead-bodies through the reaction flow passage part). See column 8, lines 56-61 and Figures 2A and 3A. Harrison et al also teach that the solid phase extraction material in zone 35 are beads with antibody on the surface that react with antigen in solution (i.e. bead-bodies with antibodies fixed thereon). See column 12, lines 35-40. Harrison et al furthermore teach that light generated from an enzyme reaction is detected, wherein the detection is downstream from the enzyme bed (i.e. enzyme reaction products are detected in the detection flow passage part). See column 13, lines 4-7; and column 13, line 64 to column 14, line 4.

However, Harrison et al fail to teach that the enzyme reaction product is produced by antigen antibody reaction with an enzyme, wherein the enzyme is in solution and the antigen antibody reaction is on bead-bodies.

Eteshola et al teach the downstream detection of a fluorophore in a microfluidic device, wherein the fluorophore is generated from an HPR-catalyzed fluorogenic substrate conversion, in order to provide a fast, simply, and sensitive immunoassay that does not require a multistate, labor-intensive process with long incubation periods and

washes. See page 129, left column, 2nd paragraph to right column, 1st paragraph; and page 130, right column, 3rd paragraph to page 131, left column, 1st paragraph; and Figure 1 and caption.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus and method of Harrison et al with the downstream detection of a fluorophore in a microfluidic device, wherein the fluorophore is generated from an HPR-catalyzed fluorogenic substrate conversion, as taught by Eteshola et al, in order to provide a fast, simply, and sensitive ELISA that does not require a multistate, labor-intensive process with long incubation periods and washes. The efficiency of HPR-catalyzed fluorogenic substrate conversion, as taught by Eteshola, provides the motivation to combine the mobile enzyme and immobilized antibody technique of Eteshola with the method of Harrison et al. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the downstream detection of a fluorophore in an ELISA, as taught by Eteshola et al, in the apparatus and method of Harrison et al, since Harrison et al teach a microfluidic device with antigen capture for immunoassays and downstream detection, and the fluorophore production and detection of Eteshola et al is also in a microfluidic device with antigen capture and means for downstream detection.

6. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harrison et al (US 6,432,290 B1) in view of Eteshola et al (Sensors and Actuators B, 2001) and Sato et al (Analytical Sciences, 1999).

Harrison et al reference has been disclosed above, but fail to teach detection by a thermal lens microscope system in the detection flow passage part.

Sato et al teach a thermal-lens microscope to detect optical irradiation in a microfluidic channel, in order to provide a means of optical detection with ultrahigh sensitivity and stability. See page 526, left column, 1st paragraph to right column, 1st paragraph; and Figure 1 and caption. In addition, Sato et al teach applications of the thermal-lens microscope to enzyme and immunoassays. See page 525, left column, 2nd paragraph,

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Harrison et al with a thermal-lens microscope to detect optical irradiation in a microfluidic channel, as taught by Sato et al, in order to provide a means of optical detection with ultrahigh sensitivity and stability. The effectiveness of the thermal-lens microscope, as taught by Sato et al, provides motivation to combine the microscope with the detection method of Harrison et al. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a thermal lens microscope, as taught by Sato et al, in the apparatus of Harrison et al, since Harrison et al teach a detection channel and detection means to detect enzyme reactions that give off light, and the thermal lens microscope of Sato et al performs detection by through optical irradiation of enzyme reactions.

Response to Arguments

7. On pages 4-9 (i.e. Remarks) of the response filed June 9, 2006, Applicants traverse the rejection of claim 20 under 35 U.S.C. 102(e) as being anticipated by Harrison et al, and the rejection of claim 21 under 35 U.S.C. 103(a) as being unpatentable over Harrison et al over Eteshola et al and Sato et al. Specifically, Applicants present three arguments focusing on Harrison et al reference since it is the primary reference in both claims:

(1) Applicants contend that the added limitations to claims 20 and 21 provide a structural limitation that overcomes the applied art by requiring the arrangement of the reaction flow passage part and the detection flow passage part so that a majority of enzyme reaction products reach the detection flow passage part. See page 5, 2nd-5th paragraphs.

(2) Applicants argue that solvent flow in Harrison et al passes mainly along a cover plate, thereby not being able to contact liquid in chamber (4) in between the weirs. See page 6, 3rd paragraph. Applicants also state that since the elution solvent is provided from a stream at weir 6e and exits collection (4) at weir 6f, only a little part of concentration protein digest makes it to the stage of final analysis. See page 6, last paragraph spanning to page 7, 1st paragraph. Applicants conclude this point with the statement that the majority of beads (12) in chamber (4) cannot contribute to an increase in signal strength since a

majority of the labeled reagent and a majority of the beads do not reach the detector. See page 7, 2nd paragraph.

(3) Applicants contend that Harrison et al teach side channel (5) is indispensable with chamber (4) and such a structure is different from the present invention. See page 7, 3rd paragraph.

Applicants' arguments have been fully considered, but are not persuasive in overcoming the applied references.

In regards to Applicants' first argument (1) above, although the added limitations require a structural embodiment, that embodiment is recited in extremely broad language that allows Harrison et al reference to continue to read on the claims. The limitation recites "wherein the ***reaction flow passage part*** and the ***detection flow passage part are arranged so that***..." The term "arranged" does not provide for a specific arrangement between the reaction flow passage part and the detection flow passage part, thereby rendering the claims to only require an apparatus with said parts having the capability of producing the increased signal strength. Since Harrison et al teach both parts, in the form of channel 37 (i.e. reaction flow passage part) and collection channel 40 (i.e. detection flow passage part), and both are "arranged" in a manner with respect to one another, the reference fully anticipates the limitation.

In regards to Applicants' second argument (2) above, the presence of weirs that confine beads within a chamber and allow only a small space for liquid flow do not necessarily prevent liquid from encountering all of the beads within the chamber. In

fact, Harrison et al teach that beads having immobilized protein A thereon and packed within a chamber are exposed to a fluid flow of antitheophylline antibodies that bind to protein A, and that the beads are **saturated** with the antibodies after several minutes. See column 12, lines 52-67. The beads can only be saturated if liquid comes into contact with all of the beads, thereby indicating that fluid does not flow only along the cover of the apparatus, as argued by Applicants. By being able to saturate the beads with binding reagents, Harrison et al therefore disclose that a majority of the beads are involved with the reactions by having antibody-antigen complexes thereon. Furthermore, Harrison et al teach that labeled theophylline can then be introduced into the chamber by liquid flow and that the beads are once again saturated with the labeled antigen, thereby providing a protein A-antitheophylline-labeled theophylline complex. See column 13, lines 2-9. The complex is then exposed to a chaotropic agent that elutes the theophylline from the beads, which is then detected downstream. See column 13, lines 9-19. Since the bead/chamber/weir arrangement is capable of allowing complete saturation of binding sites on the beads, this arrangement is therefore also fully capable of exposing all of the complexes with the chaotropic agent, which would then cleave all of the theophylline to thereby provide a majority of labels downstream to the detector.

In further regards to Applicants' second argument (2) above, since weirs 6e and 6f form the last chamber 35 prior to the collection chamber, the elution buffer is necessarily provided at the last stage of reaction prior to analysis. All biomolecules

within chamber 35 would therefore be in contact with the elution buffer and a majority of the labels would necessarily be eluted and sent to the collection chamber.

In regards to Applicants' third argument (3) above, the fact that channel 5 and chamber 4 may be indispensable in Harrison et al's device and different from the present invention as depicted in the Drawings of the instant application or absent from the instant claims does not prevent Harrison et al's apparatus from reading on the claimed invention since the claims have "comprising" language (line 2 of both claims 20 and 21) that allow additional components to be present in the claimed chip.

In light of the statements above, Applicants' arguments are not found convincing and the claims remain rejected.

Conclusion

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leon Y. Lum
Patent Examiner
Art Unit 1641

LONG V. LE 08/18/06
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

LYL